pathogenicity research. This model relies on nanoarray and microarray detection techniques for the generation of data on physiological responses to infection. The studies extend the usefulness of an existing rabbit anthrax model, and should accelerate the development of countermeasures against anthrax. Protein microarray technology will be utilized and a collection of approximately 5000 ORF clones from *B. anthracis* will be transferred into expression vectors, tested for protein expression, and purified proteins will be used to generate protein microarrays. Arraying procedures and validating genomic proteins will follow Invitrogen-established technologies. Arrays will be evaluated on samples from experimentally infected rabbits to potentially yield significant new data for pathogenicity, vaccine development, and therapeutic antimicrobial trials. The new model is expected to yield carefully defined, reproducible data useful with the Food and Drug Administration's animal rule.

[0271] Protein microarrays contain defined sets of proteins arrayed in up to 20,000 nano-dots on microscope-sized slides. It is not practical for bacteria like *Bacillus anthracis*, which encode thousands of proteins, to analyze each protein one at a time. The advantage of protein arrays is the ability, in a single experiment, to rapidly and simultaneously screen large numbers of proteins for biochemical activities, immunogenicity, protein-protein interactions, etc.

[0272] As noted above, the first commercially viable "whole-proteome" microarray was launched by Invitrogen Corporation in 2004. Although various protein arrays have been produced in research labs, for reproducible data, the arrays have to be produced: (1) employing rigorous quality control on the cloned genes to ensure sequence identity to reference databases; (2) using purified proteins checked for proper concentration and molecular weight; (3) using an appropriate expression host that allows post-translation modifications; (4) utilizing buffers and conditions to ensure non-denatured proteins; and (5) incorporating varied controls on each slide manufactured according to commercially acceptable specifications.

[0273] The New Zealand White rabbit is a convenient model for study using both the subcutaneous and inhalation exposure routes. This rabbit model has been used for anthrax vaccine efficacy testing, anthrax post-exposure prophylactic efficacy, and for anthrax therapeutic intervention studies. With both exposure routes, the survival rates and time-to-death of the naïve controls are very similar. Challenge doses usually approximate 100-200×LD_{50} and survival rate of naïve controls is about 1% overall. Time-to-death in both models is about 5 days. Serial blood sampling to examine the proteins that are expressed during the course of infection and to characterize the overall response to the bacterial proteins can be performed over the entire course of the disease. In order to generate an antibody response, a sub-lethal dose or promotion of partial protection will be required. Partial protection can be assessed through the use of levofloxacin post-challenge, an antibody administered post-challenge, or a general use prophylaxis of Anthrax Vaccine Adsorbed ("AVA") to protect rabbits prior to challenge.

[0274] These arrays may be exploited by closely integrating them into an animal model with the hope of achieving a significant increase in the amount and quality of data obtained in the rabbit anthrax model. A collection of approximately 5000 ORF clones from *B. anthracis* will be transferred into expression vectors, tested for protein expression, expression-validated clones will be used to generate protein microarrays, and these arrays will be validated. The protein microarrays can be used to: (1) discover, in unprecedented detail, knowledge of the quantity and quality of the humoral immune response; (2) target, for antimicrobial development, protein-protein interactions that occur between host and pathogen; and (3) expand the knowledge of molecular pathogenicity of *B. anthracis*. These arrays could provide significant new knowledge to accelerate the development of new vaccines, therapeutics and diagnostic assays.

[0275] Baseline immuno-reactivity data will be established by analyzing on arrays sequentially collected sera from *B. anthracis* infected rabbits. Samples would come from terminally ill animals, any surviving animals and controls. Animals infected by aerosol route will be compared with those infected by injection. The immunological profile (IgG, IgM) to each of the thousands of arrayed proteins will be established using rabbits immunized with established anthrax vaccines. The immunological events associated with survival of animals treated at various times post-inoculation with an antimicrobial drug will be established.

[0276] Microarrays hold the potential to gather a significant increase of new information from each sample, and thus would greatly expand the usefulness of the limited animal models available for biothreat agents. For high containment diseases, research is particularly slow and complicated. For many diseases, there are few if any readily available antimicrobials. Knowledge from studies in this model should lead to advances in the basic understanding of the virulence of *B. anthracis*, and consequently aid the development of antimicrobials. In those cases where a putative antimicrobial exists, often the mechanism of action is difficult to uncover. Using arrays to analyze an animal's response to infection with or without an antimicrobial could yield information on how the animal processed the infection while being treated. In regard to vaccinology, there are a number of potential anthrax vaccines under development. The ability of microarrays to quickly provide extensive comparative data from different vaccines could be very significant. Understanding the quantity and quality of the protective response these vaccines generate is of paramount importance during development.

[0277] From the description provided herein, one skilled in the art can readily ascertain the essential characteristics of this invention, and without departing from the spirit and scope thereof, can make various changes and modifications of the invention to adapt it to various usages and conditions without undue experimentation. All patents, patent applications and publications cited herein are incorporated by reference in their entirety.

1. A composition comprising ten or more proteins, each of which shares at least 10 amino acids of sequence identity with different proteins derived from one or more pathogenic agent,

wherein the proteins are each located in separate locations on a solid support.

2. The composition of claim **1**, wherein the pathogenic agent is one or more pathogenic agents of a class selected from the group consisting of a protozoan, a virus, a viroid, a bacterium, and a parasitic worm.

3. The composition of claim **1**, wherein the solid support contains from about two to about four thousand proteins, from about two to about three thousand proteins, from about two to about two thousand proteins, from about two to about one thousand proteins, from about one hundred to about five